FORM PTO-1390 (REV 12-29-99)

U S DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER: 33013-2

U S. APPLICATION NO (If known, see 37 CFR 1 5): 09/623884

INTERNATIONAL APPLICATION NO	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/GB99/00742	12 March 1999	12 March 1998

TITLE OF INVENTION: CAPILLARY ELECTROPHORESIS DEVICE

APPLICANT(S) FOR DO/EO/US: HASSARD, JOHN

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. [X] This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. [ ] This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. [X] This express request to begin national examination procedures (35 U.S.C. 371(f) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C371(b) and PCT Articles 22 and 39(1)
4. [X] A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. [X] A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. [ ] is transmitted herewith (required only if not transmitted by the International Bureau).
   b. [X] has been transmitted by the International Bureau.
   c. [ ] is not required, as the application was filed in the United States Receiving Ofice (RO/US).
6. [ ] A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. [X] Amendments to the claims of the International Application under PCT Article 19(35 U.S.C. 371(c)(3))
   a. [ ] are transmitted herewith (required only if not transmitted by the International Bureau).
   b. [ ] have been transmitted by the International Bureau.
   c. [ ] have not been made; however, the time limit for making such amendments has NOT expired.
   d. [X] have not been made and will not be made.
8. [ ] A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. [X] An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). (unsigned)
10. [ ] A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern document(s) or information included:

11. [ ] An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. [ ] An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. [X] A FIRST preliminary amendment.
    [ ] A SECOND or SUBSEQUENT preliminary amendment.
14. [ ] A substitute specification.
15. [ ] A change of power of attorney and/or address letter.
16. [X] Other items or information: PCT Request (RO/101)
    Published Specification (WO-99/46590)

"Express Mail" label number EM544390025US
Date of Deposit September 11, 2000
I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR S1.10 on the date indicated above and is addressed to Commissioner for Patents, Washington, D.C. 20231-9999.

Signature of person mailing paper or fee

U.S. APPLICATION NO. (if known, see 37 CFR 1.5)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
09/623884	PCT/GB99/00742	33013-2

17. [X] The following fees are submitted:

BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)) :

Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO **$970.00**

International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO **$840.00**

International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO **$690.00**

International preliminary examination fee paid to USPTO (37 CFR 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4) **$670.00**

International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4) **$96.00**

	CALCULATIONS PTO USE ONLY	
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 840.00	
Surcharge of **$130.00** for furnishing the oath or declaration later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(e)).	$	

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
Total claims	17 - 20 =	0	X **$18.00**	$ 0	
Independent claims	1 - 3 =	0	X **$78.00**	$ 0	
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ **$260.00**	$ 260.00	
TOTAL OF ABOVE CALCULATIONS =				$ 1100.00	
Reduction of 1/2 for filing by small entity, if applicable. A Small Entity Statment must also by filed (Note 37 CFR 1.9, 1.27, 1.28).				$	
SUBTOTAL =				$ 1100.00	
Processing fee of **$130.00** for furnishing the English translation later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(f)). +				$	
TOTAL NATIONAL FEE =				$ 1100.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). **$40.00** per property +				$	
TOTAL FEES ENCLOSED =				$ 1100.00	
				Amount to be refunded:	$
				charged:	$

a. [X] A check in the amount of $ 1,100.00 to cover the above fees is enclosed.

b. [ ] Please charge my Deposit Account No. _____ in the amount of $_____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. [X] The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 23-3030. A duplicate copy of this sheet is enclosed.

(but not issue fees)

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pendin g status.

SEND ALL CORRESPONDENCE TO

J. Andrew Lowes

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317-634-3456

SIGNATURE

J. Andrew Lowes

NAME

40,706

REGISTRATION NUMBER

33013-2:JAL:kkb 100411

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re patent application of:	)	
	)	Before the Examiner
John Hassard	)	
	)	(Unknown)
Serial No. (Unknown)	)	
	)	Group Art Unit
Filed September 11, 2000	)	
	)	(Unknown)
CAPILLARY	)	
ELECTROPHORESIS DEVICE	)	September 11, 2000

Express Mail label No. EM544390025US
I hereby certify that this correspondence is being deposited with the United States Postal Service as Express Mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231 on

September 11, 2000
(Date of Deposit)

J. Andrew Lowes
Name of Registered Representative

Signature

September 11, 2000
Date of Signature

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Prior to examination, please enter the following amendments in the specification. Additionally, please charge any deficiency in fees due or apply any overpayment credit to Deposit Account No. 23-3030, but not to include any issue fees.

IN THE SPECIFICATION:

On page 1, after the title, please insert the following paragraph:

--This application claims the benefit of PCT Application No. PCT/GB99/00742, filed March 12, 1999.--.

On page 1, line 6, please insert --BACKGROUND OF THE INVENTION--.

On page 2, line 1, please insert --SUMMARY OF THE INVENTION--.

On page 3, line 2, please insert --BRIEF DESCRIPTION OF THE DRAWING--.

On page 3, line 15, please insert --DESCRIPTION OF PREFERRED EMBODIMENT--.

On page 7, line 2, please insert --What is claimed is:--.

REMARKS

Applicants respectfully request consideration of this Application and Preliminary Amendments. The undersigned would welcome a telephone call from the Examiner if there remain any further issues with respect to the form of the application.

Respectfully Submitted,

By: J. Andrew Lowes

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CAPILLARY ELECTROPHORESIS DEVICE

This invention relates to analysers. Embodiments of the invention relate to instruments for the determination of molecular characteristics, such as the length of nucleic acid in terms of base pairs, and the sequencing of genetic samples.

There are several current techniques for analysing materials such as DNA samples in an automated or semi-automated manner. One such technique which has been demonstrated for DNA analysis is the use of so-called microfabricated capillary electrophoresis (CE) chips.

These devices comprise a substrate in which a number of very fine capillary channels are etched and filled with a gel material. A material to be analysed passes along the capillary channel under the influence of an electric field. Components of the material - for example, nucleic acids - progress along the channel at different rates depending on the relative molecular weights of the components, leading to a separation by molecular weight.

Current techniques use photographic techniques to image radioactive or luminescent tags attached to the nucleic acids. This is a time consuming process. A quicker but expensive alterative is to use phosphor imagers to record the sequences. Furthermore, both processes use hazardous chemicals to tag the nucleic acids and the safe use and disposal of these is a major problem, requiring skilful scientific and technical input.

As mentioned above, all of these techniques are relatively slow. In any current emission technique, such as CE-laser induced fluorescence (CE-LIF) the time-to-sequence depends on the separation gradient (i.e. the electric field) and the discriminator power (e.g. the capillary or electrophoresis gel) convolved with the size of the objects to be separated.

There is a need for an improved technique offering a faster response than current techniques and avoiding the use of hazardous materials.

PCT/GB96/01121 discloses an electrophoresis system in which material components are driven along quartz tubes. In effect, the shadow of the separated components is detected by directing an ultraviolet (UV) light from one side of the tubes towards a detector at the other side.

This invention provides an analyser comprising: a substrate of diamond, sapphire or a polymer material; an array of one or more elongate capillary channels formed in the substrate; means for driving a sample to be tested along one or more of the channels whereby the velocities of components of the sample along the channels depends on the relative molecular weights of those components; a radiation source and a radiation detector disposed on either side of the channel array so as to detect the presence of material in the channels as interruptions in the radiation path between the radiation source and the radiation detector.

The invention addresses the above problems by providing a new selection of substrates offering many advantages over the glass, quartz and plastics of previous analysers. In particular, the whole apparatus can be miniaturised and the use of hazardous markers is avoided by detecting the "shadow" of separated components (e.g. DNA fragments).

Embodiments of the invention can provide an analysis technique which can be carried out while avoiding the use of mutagenic, toxic and carcinogenic chemiluminescent, bioluminescent and radiolabels, with associated benefits in running costs, safety and ease of disposal.

Embodiments of the invention can provide up to an order of magnitude increase in speed for DNA sequencing. For example, a sequence of 500 base pairs which might take 6 hours using a conventional electrophoresis technique could be achieved in 10 minutes using a prototype embodiment of the invention. The saving in time can arise because in current imaging techniques the images of bands identified by conventional labels is heavily smeared by the isotropic emission characteristics of the labels, whereas in embodiments of the present invention the image of a nucleic acid band is substantially the same size as the band, smeared only by diffraction.

Embodiments of the invention can further provide an improved detection sensitivity and signal-to-noise ratio in sub-microlitre sequencing and imaging.

Embodiments of the invention can allow pre-programmed sequence recognition masks to accompany an installation, so that in principle a "yes-no" answer could be obtained by relatively untrained end-users. A sequence triage system results which, coupled to the potentially low cost of this technology, could result in the use of apparatus according to embodiments of the invention in doctors' surgeries, schools

and even on individual researchers' desks.

Embodiments of the invention will now be described, by way of example only, with reference to the accompanying drawings in which:

Figure 1 is a schematic perspective view of part of an analyser according to an embodiment of the invention;

Figure 2 is a schematic plan view of an array of analyser channels according to an embodiment of the invention;

Figure 3 is an enlarged view of two supply wells;

Figure 4 is a schematic cross sectional view of an analyser operating at a UV wavelength of about 260 nm;

Figure 5 is a schematic cross sectional view of an analyser channel operating at a UV wavelength of about 200 nm; and

Figure 6 is a schematic graph illustrating the signal to noise performance of prototype embodiments of the invention.

Referring now to Figure 1, an analyser according to embodiments of the invention comprises an array of channels 10 formed as the substrate is grown or deposited (e.g. by CVD) or etched by excimer laser ablation into a substrate 20 of diamond, sapphire (preferably coated in nanocrystalline diamond) or polymer, possibly deposited on a substrate of a material such as silicon. The channels are at least partially filled by a polyacrylimide gel and are subjected to an electric field along a longitudinal channel direction.

Under the influence of the electric field, DNA samples injected at one end of a channel progress along the channel. Components of the sample progress at a velocity dependent on the molecular weight (often expressed as a number of "base pairs" for DNA samples) of the component.

Ultraviolet light from a light source (not shown in Figure 1) is directed onto the channels, and transmitted light is imaged by a pixel array 30 of ultraviolet light detectors at the other side of the channels, in effect imaging the shadows of DNA components or bands as they pass along the channels.

At a wavelength of 253.9 nm, a mercury lamp can conveniently be used as the light source.

Each channel is less than 250 μm deep (preferably about 150 μm deep), less

than 200 μm wide (preferably 50 μm wide) and 18 mm long. The DNA samples are driven by the electric field from one end of the channel towards the other, and then the polarity of the electric field is reversed so as to drive the samples in the other direction. This process is repeated many times - e.g. several hundred times and the results averaged.

Results can be obtained by detecting the times at which fragments pass a particular point in the channel, or alteratively by performing a Fourier or other transform on the combined output of the array of spaced pixel detectors to detect velocities along the channel directly (see PCT/GB98/00645). The output of the analyser is thus a velocity map or distribution, whereby lower weight fragments have a higher velocity along the channels than higher weight fragments. Alternatively, an image of the separated components can be generated using an array of pixel detectors, as in PCT/GB96/01121 and analysed directly.

A polymer or diamond lid can be positioned over the channels to avoid contamination.

Figure 2 is a schematic plan view of an array of channels embodied on a substrate about 20 mm x 20 mm in area. A high voltage (HT) source 40 is connected to a tree structure of electrodes 50 at each end of the channels so that an electric field is applied along each channel. Typically the potential difference between ends of the channels may be about 3 kV.

Supply wells 60 are provided to inject DNA samples into each of the channels. An enlarged view of some supply wells is provided in Figure 3, showing that they are formed as substantially circular areas of etched material connected to the channels. They can be filled with a robotic micropipette apparatus available from Evotec GmbH.

So, Figure 2 shows an array of a large number of parallel separation electrophoresis microchannels with associated dendritic branching to and from a buffer well with DNA input and output wells on each channel. DNA may be switched between wells and separation channels using electric fields from suitably positioned electrodes (not shown). In the separation channels it is separated under an electric field as it permeates the electrophoresis gel in the channel - which might be nominally agarose of poly (acrylimide) but other materials are also suitable, such as

alcogel or hydrogel, so that individual lines corresponding to lengths of DNA become distinct.

Flushing the equipment can be carried out rapidly between input plugs. It is also relatively easy to input a solution to multiple plugs.

Figures 4 and 5 schematically illustrate two embodiments of the invention in cross section, one for use at a UV wavelength of about 200 nm (Figure 4) and one for use at about 260 nm, possibly 253 nm using light from a mercury lamp (Figure 5).

In each case, channels 10 are etched into a diamond substrate 20. A UV source 100 operating at the relevant wavelength is positioned so as to direct UV light onto the analyser.

In Figure 4, the lower surface 110 of each channel is made at least partially non-transparent by a treatment such as hydrogenation. When UV light impinges on the surface 110, electron-hole pairs are generated. These can be detected as a photocurrent I by connecting a dc voltage between the surface 110 and a deposited metal layer on a top surface 120 of the substrate. The resulting photocurrent can then be amplified by an amplifier 130.

The signal connections can be made to the surface 110 by depositing an electrically conductive track up the inside of each channel.

The calculation or detection of the concentration of material components between the source and the detector is relatively straightforward, being the difference in detected light levels with and without the band in the way. This is carried out by data processing apparatus such as a general purpose computer (not shown) arranged to receive the output from the detectors.

The source and/or detector can be at a single position with respect to each channel, or can be formed as an array of pixel detectors to image multiple positions on each channel at once.

The advantages of operation at 200 nm are that the absorption of the light by the DNA fragments is about 10 times higher than that at 253 nm. However, this is weighed against the convenience of operation at 253 nm as a simple source (the mercury lamp) can be used.

Figure 5 shows a similar arrangement for operation at 253 nm (or, for

example, at any wavelength near to 260 nm). Here, a confocal focusing arrangement is used, whereby a microlens fashioned during the etching process onto a diamond lid 130 between each channel and the UV source 100 acts to focus the incident light through the contents of the channels and onto a metallised area 140 at the other face of the diamond substrate. Alternatively, of course, if the positions of the source and detector were swapped, the focusing formations could be formed on what is drawn as the underside of the substrate. Again, electron-hole pairs are created and a photocurrent can be detected by applying a potential difference between a metallised layer 120 and the metallised area 140.

The systems of Figures 4 and 5 can be operated at different wavelengths, and in particular the system of Figure 4 could be operated at about 200 nm and that of Figure 5 at about 260 nm.

Diamond as a substrate has a number of particular advantages:

(i) it is chemically inert, hydrophobic and easily cleaned, e.g. using nitric acid;

(ii) it has good thermal conductivity, about 5 times better than copper, so that in embodiments of the invention the entire analyser can be cooled by a Peltier cell at one face of the device;

(iii) it is relatively transparent to UV light, and in particular is one of the most transparent materials known at 257 nm;

(iv) its surface can be made non-transparent when required, e.g. by hydrogenation;

(v) it has a high breakdown voltage - at least 10^7 Vcm^{-1};

(vi) it has a very high refractive index, so that surface or other features formed in the diamond can provide at least partial light concentration.

Figure 6 is a schematic graph showing the signal to noise (S/N) performance obtainable with embodiments of the invention. A signal to noise ratio of 20:1 is obtained for 2 ng / μL DNA.

CLAIMS

1. An analyser comprising:

a substrate of diamond, sapphire or a polymer material;

an array of one or more elongate capillary channels formed in the substrate;

means for driving a sample to be tested along one or more of the channels whereby the velocities of components of the sample along the channels depends on the relative molecular weights of those components;

a radiation source and a radiation detector disposed on either side of the channel array so as to detect the presence of material in the channels as interruptions in the radiation path between the radiation source and the radiation detector.

2. An analyser according to claim 1, in which the substrate is formed of diamond.

3. An analyser according to claim 1, in which the substrate is formed of sapphire having a coating of nanocrystalline diamond.

4. An analyser according to any one of claims 1 to 3, in which the channels are less than 250 μm deep.

5. An analyser according to claim 4, in which the channels are less than 150 um deep.

6. An analyser according to any one of the preceding claims, in which the channels are less than 200 μm wide.

7. An analyser according to any one of the preceding claims, in which the channels are less than 100 μm wide.

8. An analyser according to any one of the preceding claims, in which the radiation source comprises an ultraviolet light source.

9. An analyser according to claim 8, in which the ultraviolet light source is operable to generate ultraviolet light at a wavelength of about 260 nm or about 200 nm.

10. An analyser according to claim 8 or claim 9, in which focusing formations are formed on the substrate to at least partially focus the ultraviolet light onto the interior of each channel.

11. An analyser according to claim 10, in which the focusing formations, the channels and the radiation detector are arranged so that the interior of each channel is substantially mid-way between the focusing formations and the radiation detector.

12. An analyser according to any one of the preceding claims, in which the substrate of diamond, sapphire or a polymer is formed on a further substrate of a semiconductor material, the radiation detector being fabricated on the further substrate of semiconductor material.

13. An analyser according to claim 12, in which the semiconductor material is silicon.

14. An analyser according to claim 11 or claim 12, in which the radiation detector comprises an array of pixel detectors formed on the further substrate.

15. An analyser according to any one of claims 1 to 11, in which the radiation detector comprises an array of obscured regions on the substrate under the channels, and means for detecting an electric current formed by electron-hole pair generation at the obscured regions.

16. An analyser according to claim 15, in which the regions are formed at a lower surface of each channel.

17. An analyser according to claim 15, in which the regions are formed at a lower surface of the substrate substantially beneath each channel.

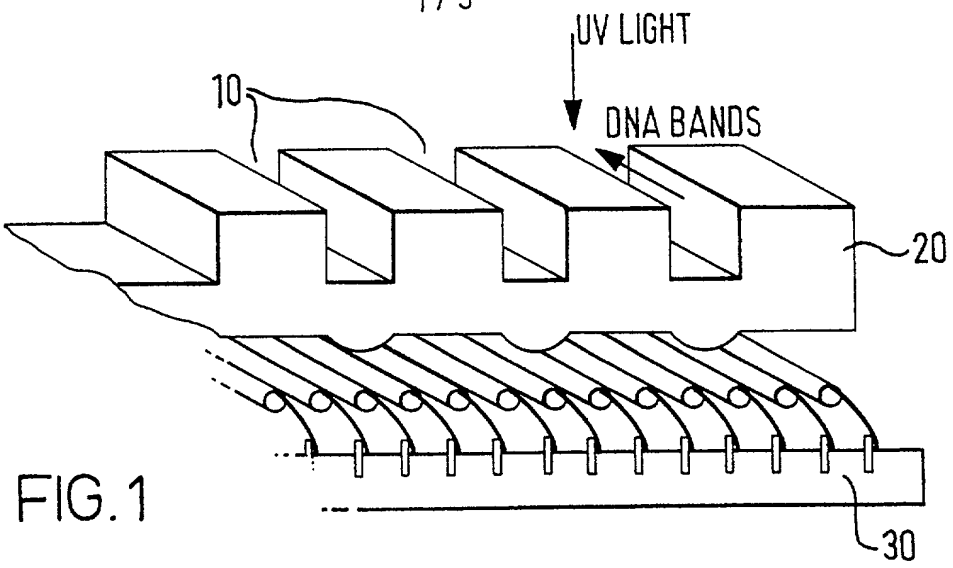

FIG. 1

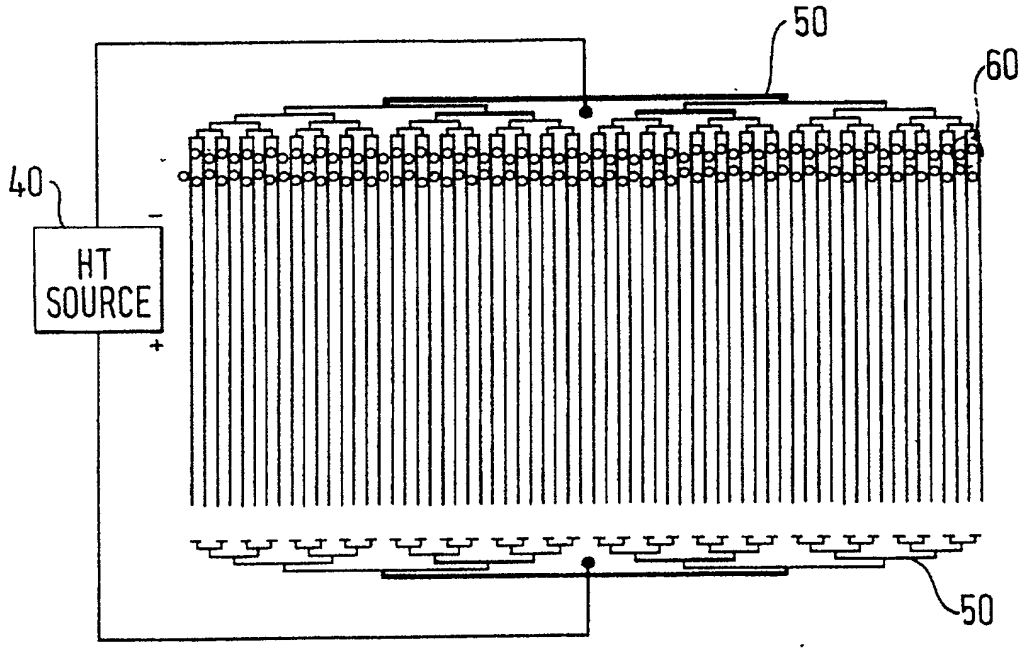

FIG. 2

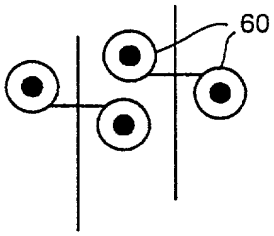
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FIG.3

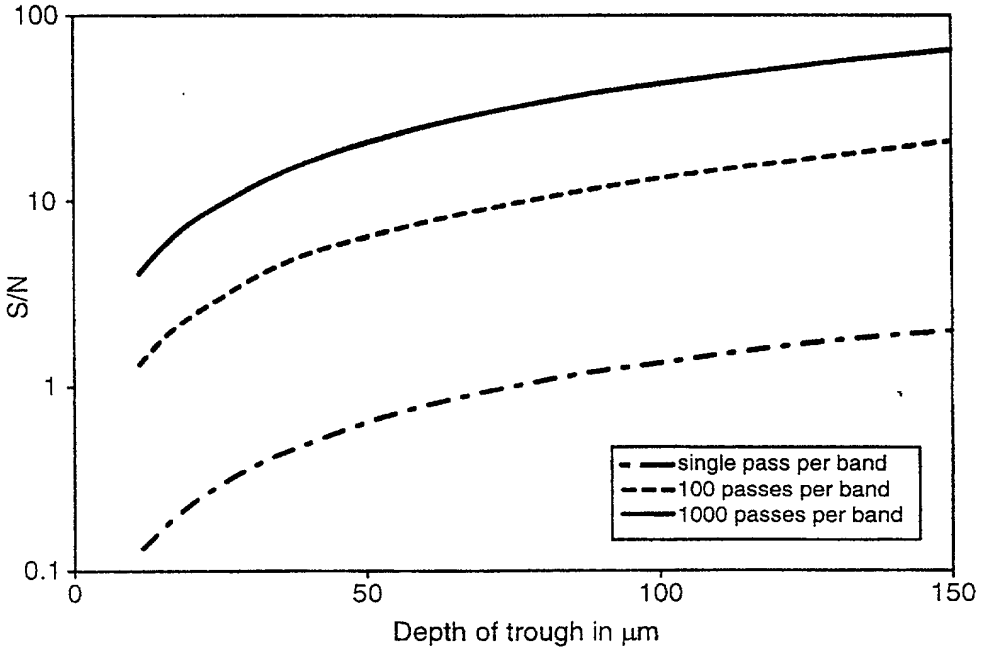
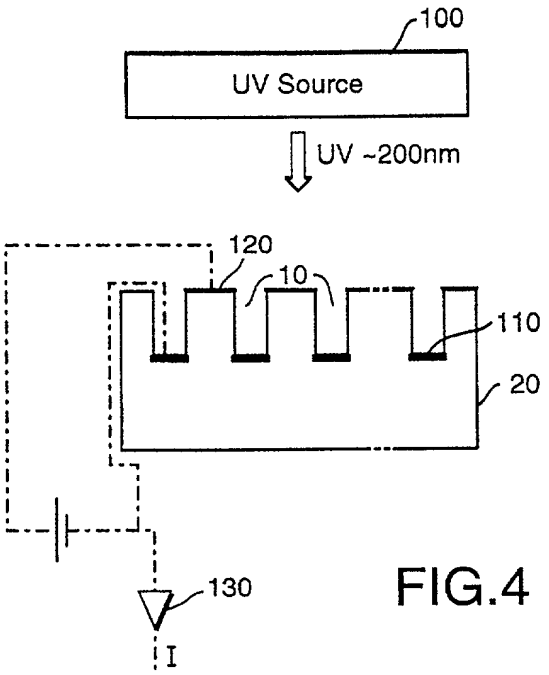

100
10
1
0.1
S/N
0
50
100
150
Depth of trough in μm
single pass per band
100 passes per band
1000 passes per band

FIG.6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120
10
110
20
130
I

FIG.4

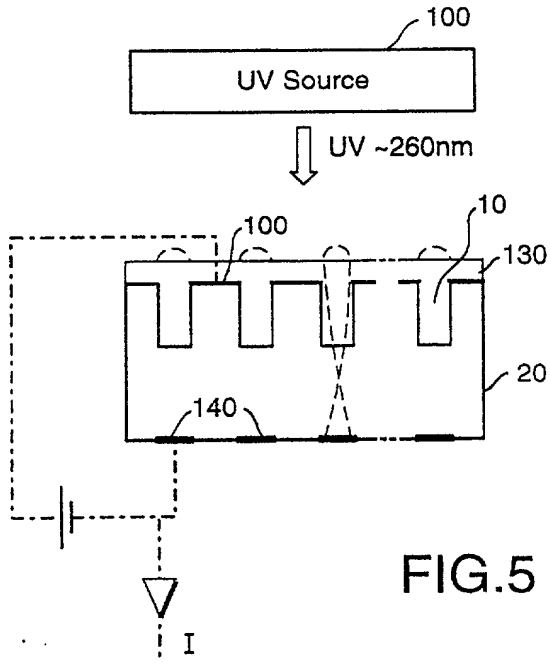
100
UV Source
UV ~260nm
100
10
130
20
140
I

FIG.5

Type a Plus sign (+) inside this box → [+]

Rec'd PCT/PTO 15 NOV 2000
09/162034

WEB/MM SB/01 (4-99)

DECLARATION FOR UTILITY OR DESIGN PATENT APPLICATION (37 CFR 1.63)

[X] Declaration Submitted With Initial Filing (*Unsigned*) **OR** [ ] Declaration Submitted after Initial Filing (surcharge 37 CFR 1.16 (e) required)

Attorney Docket Number	33013-2
First Named Inventor	John Hassard
COMPLETE IF KNOWN	
Application Number	
Filing Date	September 11, 2000
Group Art Unit	
Examiner Name	

As a below named inventor, I hereby declare that:

My residence, post office address, and citizenship are as stated below next to my name.

I believe I am the original, first, and sole inventor (if only one name is listed below) or an original, first, and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

CAPILLARY ELECTROPHORESIS DEVICE

(Title of the Invention)

the specification of which

[ ] is attached hereto **OR** [X] was filed on (MM/DD/YYYY) 03/12/1999 as United States or PCT International Application Number PCT/GB99/00742 and was amended on (MM/DD/YYYY) [ ] (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claim, as amended by any amendment specifically referred to above.

I acknowledge and hereby disclose information which is material to patentability as defined in 37 CFR 1.56.

I hereby claim foreign priority benefits under 35 U.S.C. 119 (a)-(d) or 365(b) of any foreign application(s) for patent or inventor's certificate, or 365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or of any PCT international application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application Number(s)	Country	Foreign Filing Date (MM/DD/YYYY)	Check Only If Priority Not Claimed	Certified Copy Attached? YES	Certified Copy Attached? NO
9805301.0	GB	03/12/1998	[ ]	[ ]	[X]

[ ] Additional foreign application numbers are listed on a supplemental priority data sheet PTO/SB/02B attached hereto:

I hereby claim the benefit under 35 U.S.C. 119(e) of any United States provisional application(s) listed below.

Application Number(s)	Filing Date (MM/DD/YYYY)	
		[ ] Additional provisional application numbers are listed on a supplemental priority data sheet PTO/SB/02B attached hereto.

DECLARATION – Utility or Design Patent Application

I hereby claim the benefit under 35 U.S.C. 120 of any United States application(s), or 365(c) of any PCT international application designating the Untied States of America, listed below, and insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of 35 U.S.C. 112, I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

U.S. Parent Application or PCT Number	Parent Filing Date (MM/DD/YYYY)	Parent Patent Number (*if applicable*)

[ ] Additional U.S. or PCT international application numbers are listed on a supplemental priority data sheet PTO/SB/02B attached hereto.

As a named inventor, I hereby appoint the following registered practioner(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith:

[ ] Customer Number *OR* [ ] → *Place Customer Number Bar Code Label Here*

[X] Registered practioner(s) name/registration number listed below.

Name	Registration Number	Name	Registration Number
J. Andrew Lowes	40,706		

[X] Additional registered practioner(s) named on supplemental Registered Practioner Information sheet PTO/SB/02C attached hereto.

Direct all correspondence to : [ ] Customer Number Bar Code Label [ ] *OR* [X] Correspondence address below

Name	WOODARD EMHARDT NAUGHTON MORIARTY & McNETT						
Address	111 Monument Circle, Suite 3700						
Address							
City	Indianapolis			**State**	IN	**ZIP**	46204
Country	US	**Telephone**	317/ 634-3456			**Fax**	317/637-7561

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Name of Sole or First Inventor: [ ] A petition has been filed for this unsigned inventor.

Given Name (first and middle [if any])	Family Name or Surname
John	Hassard

Inventor's Signature	John Hassard					Date	15 Nov 2000
Residence: City	London	State		Country	Great Britain	Citizenship	Great Britain
Post Office Address	Flat 3, Selkirk Hall, Princes Garden						
Post Office Address							
City	London	State		ZIP	SW71LU	Country	Great Britain

[ ] **Additional inventors are being name on the _____ supplemental Additional Inventor(s) sheet(s) PTO/SB/02A attached hereto.**

Type a Plus sign (+) inside this box → [+]

WENMM SB/02C (3-97)

DECLARATION

Registered Practitioner Information (Supplemental Sheet)

Name	Registration Number	Name	Registration Number
Harold R. Woodard	16,214		
C. David Emhardt	18,483		
Joseph A. Naughton, Jr.	19,814		
John V. Moriarty	26,207		
John C. McNett	25,533		
Thomas Q. Henry	28,309		
James M. Durlacher	28,840		
Charles R. Reeves	28,750		
Vincent O. Wagner	29,596		
Steve Zlatos	30,123		
Spiro Bereveskos	30,821		
William F. Bahret	31,087		
Clifford W. Browning	32,201		
R. Randall Frisk	32,221		
Daniel J. Lueders	32,581		
Kenneth A. Gandy	33,386		
Timothy N. Thomas	35,714		
Kerry P. Sisselman	37,237		
Kurt N. Jones	37,996		
John H. Allie	39,088		
Holiday W. Banta	40,311		
Troy J. Cole	35,102		
L. Scott Paynter	39,797		
J. Andrew Lowes	40,706		
Charles J. Meyer	41,996		
Darrin Wesley Harris	40,636		
Matthew R. Schantz	40,800		
Gregory B. Coy	40,967		
Lisa A. Hiday	40,036		
John V. Daniluck	40,581		
Christopher A. Brown	41,642		
C. John Brannon	44,557		
Jason J. Schwartz	43,910		
Arthur J. Usher IV	41,359		
Douglas A. Collier	43,556		
Brad A. Schepers	45,431		
R. Craig Tucker	45,165		
Scott J. Stevens	29,446		
James B. Myers	42,021		
John M. Bradshaw	P-46,573		
Charles P. Schmal	45,082		